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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/996,187	11/27/2001	Laurence McCarthy	22510-501	3934

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EXAMINER	
HILL, MYRON G	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 04/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/996,187	MCCARTHY ET AL.	
	Examiner	Art Unit	
	Myron G. Hill	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1- 34* is/are pending in the application.

4a) Of the above claim(s) *3- 6, 22- 25, 29, and 31- 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 7- 21, 26- 28, and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/10/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I in paper filed 12 January 2004 is acknowledged.

Claims 3- 6, 22- 25, 29, and 31- 34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

The following claims are under consideration: claims 1, 2, 7- 21, 26- 28, and 30.

Information Disclosure Statement

A signed and initialed copy of the IDS filed 10 December 2002 is enclosed.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 7- 21, 26- 28, and 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is not clear what the bioactive molecule is. Is it the nucleic acid of 1 a) or is it the product of what is encoded by the nucleic acid as recited in 1 b)? Claim 1 is also not a complete method. It is suggested that "evaluating" be changed to "evaluating the phenotype" in the preamble, and that "bioactive molecule" be changed to "produced bioactive molecule" in part d). It is also

not clear what the method is intended to result in. This is because it is not clear that the preamble reflects the steps of the method because the steps (which lack a conclusion) evaluate the phenotype of the bioactive molecule in the presence or absence of a compound, not just assay for the phenotype.

In claims 7- 9, it is not clear what "bioactive molecule further comprising" is meant to convey. The encoding sequence would be RNA or DNA to begin with so it is not clear what is added in claim 7. In claim 8, it is not clear, if the nucleic acid is DNA, how it can comprise additional RNA.

The antecedent basis for "the amplified" in claims 12 and 13 is not clear.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 7- 21, 26- 28, and 30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for detecting the phenotype of a viral polymerase and its resistant to a compound, does not reasonably provide enablement for all disease states and bioactive compounds associated with those disease states. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims are evaluated for scope of enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows:

(1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The claims are drawn to evaluating the phenotype of a bioactive molecule associated with a disease state.

The art of screening for activity of expressed viral polyerases is extensive as shown by the many references listed in the IDS.

The scope of the invention is not limited to viral polymerases. The claims require any patient afflicted with any disease state and extracting a specimen that comprises a bioactive molecule associated with "a" disease state. The claims do not even require that the bioactive molecule be associated with the disease state the patient is afflicted with.

As defined on pages 10 and 11, a bioactive molecule encompasses just about everything. Pages 7- 10 define specific types of disease states but do not literally define the term specifically beyond the cited examples of different disease states. The definition of "disease states" is not limited to the disclosed disease states.

The section "Genetic Disease State" (pages 9 and 10) lists "absence of a gene" (page 10, line 1). The method cannot be practiced with this condition because there is

no nucleic acid that encodes a bioactive molecule and no expression product, and thus the phenotype cannot be determined in the presence or absence of a test compound.

The section "Genetic Disease State" also discloses "obesity" (page 10, line 13) as a disease state. What it the bioactive molecule that is associated with that disease?

The specification does not provide the needed bioactive molecule for all disclosed disease states, the recited method cannot work on genes that are not present.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Clearly, there is lack of guidance directing a skilled artisan to practice the instantly claimed methods. Without specific guidance or direction and /or working examples, one of ordinary skill in the art would not be able to reproducibly practice the entire scope of the invention as claimed, without undue experimentation.

Claims 1, 2, 7- 21, 26- 28, and 30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The burden of the written description requirement in this application for assaying for phenotype of bioactive molecules for all disease states has not been met.

The written description in this case only sets forth screening of viral polymerases.

Vas-Cath Inc. v. Mahurkar ((CAFC, 1991) 19 USPQ2d 1111), clearly states that "Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See Vas-Cath at page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see Vas-Cath at page 1115).

Bioactive molecules are not known for all disease states listed. As one example, the section "Genetic Disease State" also discloses "obesity" (page 10, line 13) as a disease state. Applicant has not disclosed the bioactive molecule that would be required to be amplified in order to determine the phenotype of obesity or what phenotype would indicate obesity in the recited method.

Accordingly, there is evidence that the full scope of the claimed invention was not in Applicant's possession as of the filing date sought.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 2, 7- 21, 26- 28, and 30 are rejected under 35 U.S.C. 101 because the disclosed invention is inoperative and therefore lacks utility. The claims are drawn to assaying a bioactive molecule.

The definition of bioactive includes virtually everything (pages 10 and 11) including nuclic acids and polypeptides.

The section "Genetic Disease State" (pages 9 and 10) lists "absence of a gene" (page 10, line 1).

The method cannot be practiced with this condition because there is no nucleic acid that encodes a bioactive molecule and no expression product, and thus the phenotype cannot be determined in the presence or absence of a test compound.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 7- 10, 12- 16, 19- 21, 26, 27, and 30 are rejected under 35 U.S.C. 102(a) as being anticipated by Oon *et al.* (WO 00/18958 from IDS).

The claims are drawn to a method of producing and evaluating a bioactive molecule comprising providing a nucleic acid sequence encoding the bioactive

molecule, expressing the bioactive molecule, contacting the bioactive molecule with a compound, and detecting the phenotype in the presence or absence of the compound.

Oon *et al.* teach samples can be derived from serum (page 5, line 9) and bioactive molecules can be amplified by PCR with primers that contain a promoter that can be used in *in vitro* transcription/translation reactions, and the phenotype of the bioactive molecule can be determined by the enzymatic activity of priming (page 5, lines 1- 8). The assay can also be used to test compounds for their ability to inhibit bioactive molecule phenotypic activity (page 5, lines 14- 16).

Though Oon *et al.* do not literally *ipsis verba* disclose resistance phenotype testing, drug resistant mutants were known. Oon *et al.* teach screening of bioactive molecules using known inhibitory compounds. Oon *et al.* inherently test for resistance phenotypes because when the phenotype determining assay is carried out, detecting drug resistant mutant phenotypes is clearly determined by the fact that the drug would not have an effect on the enzymatic activity of the bioactive molecule.

Therefore, Oon *et al.* anticipate the claimed invention.

Claims 1, 2, 15, 16, 19- 21, and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Lardner *et al.* (Science Vol. 246, pages 1155- 1158, from IDS).

The claims are drawn to a method of producing and evaluating a bioactive molecule comprising providing a nucleic acid sequence encoding the bioactive

molecule, expressing the bioactive molecule, contacting the bioactive molecule with a compound, and detecting the phenotype in the presence or absence of the compound.

Lardner *et al.* disclose assaying a bioactive molecule by providing a nucleic acid sequence of the bioactive molecule (an RT cloned into M13), expressing the bioactive molecule, and assaying for enzymatic activity (Zidovudine sensitivity)(Table 1 with caption).

The clone of Lardner *et al.* inherently contains regulatory elements such as promoters and an origin of replication.

Therefore, Lardner *et al.* anticipate the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 11, 17, and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lardner *et al.*, as applied above, and further in view of either Promega Catalog or Invitrogen Catalog.

The claims are drawn to a method of producing and evaluating a bioactive molecule comprising providing a nucleic acid sequence encoding the bioactive molecule, expressing the bioactive molecule, contacting the bioactive molecule with a compound, and detecting the phenotype in the presence or absence of the compound.

Lardner *et al.* disclose assaying a bioactive molecule by providing a nucleic acid sequence of the bioactive molecule (an RT cloned into M13), expressing the bioactive molecule, and assaying for enzymatic activity (Zidovudine sensitivity, Table 1 with caption).

Lardner *et al.* does not teach a cell-free prokatyotic (E. *coli*) cell lysate translation system or a nucleic acid comprising a second nucleic acid that is a purification tag.

The Promega Catalog teaches a cell-free prokatyotic (E. *coli*) cell lysate translation system (page 284).

The Invitrogen Catalog teaches a nucleic acid comprising a second nucleic acid that is a purification tag (page 5).

One of ordinary skill in the art at the time of invention would have been motivated to modify the method of Lardner *et al.* with the system of Promega because Promega teaches that this system allows for fine mapping, and rapid verification of *in vitro* generated mutants because the products are not cloned and the expressed product can be analyzed *in vitro*. One of ordinary skill in the art at the time of invention would have used Promega because not cloning and *in vitro* analysis would save time and Lardner *et al.* requires the analysis of many isolates which are analyzed *in vitro* for change of phenotype enzymatic activity of the bioactive molecule.

One of ordinary skill in the art at the time of invention would have been motivated to modify the method of Lardner *et al.* with the system of Invetrogen to purify expressed proteins because the system of Invetrogen saves time and money because the system exploits the selective binding properties of the purification tag thereby eliminating the need to develop purification protocols for each different protein. One of ordinary skill in the art at the time of invention would have known that the sequence that encodes the tag is added to the nucleotide sequence that comprises the expressed bioactive molecule and is translated along with it to make a protein that can be purified.

Thus, it would have been *prima facie* obvious to modify the method of Lardner *et al.* with the methods of the Promega Catalog or Invitrogen Catalog with the expectation of success in practicing the method of Lardner *et al.* without cloning and using a tag to purify the protein of Lardner *et al.*

Conclusion

No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Myron G. Hill whose telephone number is 571-272-0901. The examiner can normally be reached on 9am-6pm Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Myron G. Hill
Patent Examiner
April 16, 2004

JEFFREY STUCKER
PRIMARY EXAMINER